REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 12–13, 21, 24–37, and 39-40 are requested to be cancelled.

Claims 1 and 14 are currently being amended.

Claims 41–44 are being added.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1–11, 14–20, 22–23, 38, and 41–44 are now pending in this application.

Applicants thank the examiner for duly completing the form PTO/SB/08A and considering the references cited therein.

I. The Objection Due To "Butylated Hydroxyanisole"

This rejection has been obviated by canceling claim 32. The Office objected to claims 1, 4, 5, 14, and 32 because the terms "BHA" and "butylated hydroxyanisole" appeared separately in those claims, and the Office suggested defining these terms as identical in claim 1. Applicants disagree with this objection, however the only occurrence of "butylated hydroxyanisole" is in claim 32, which is now canceled. Accordingly, the rejection has been obviated.

II. The Rejection Under 35 U.S.C. § 112

This rejection has been obviated by canceling claim 40.

The Office rejected claim 40 under § 112 for alleged lack of enablement in the specification. Applicants disagree with this rejection and reserve the right to pursue the subject matter of claim 40 in a continuation or divisional application. However to further prosecution, Applicants have canceled claim 40 to obviate the rejection.

III. The Rejection Under 35 U.S.C. § 103(a)

The Office rejects claims 1-40 under § 103(a) over U.S. Patent No. 5,846,966 ("Rosenblum et al."); U.S. Patent No. 6,372,255 (Saslawski et al."); WO 96/09827; U.S. Patent No. 6,420,217; the Handbook of Pharmaceutical Excipients; and the STN Registry File for Ezetimibe. The Office maintains that Rosenblum et al. suggests compositions including both ezetimibe and simvastatin in a variety of dosage forms and levels (Office Action, pp. 5 – 6). The Office recognizes that Rosenblum et al. differs from the claims in failing to disclose BHA, other required compounds, and the claimed proportions of ingredients (Office Action, sentence bridging pp. 6 – 7). The Office states that Rosenblum et al. discloses antioxidants, and therefore a person of ordinary skill in the art would have been motivated to include BHA, and the Office cites Saslawski et al. for its disclosure of BHA as antioxidant; the Office also states that Rosenblum et al. discloses that the formulation may include conventional pharmaceutical excipients and therefore a person of ordinary skill in the art would have been motivated to include any such excipients in corresponding formulation (Office Action, p. 7, last paragraph).

Applicants have canceled claims 24 – 40, which required an HMG-CoA reductase inhibitor, thus obviating the aspect of this ground of rejection directed to this subject matter. Nevertheless, Applicants disagree with this ground of rejection of claims 24 – 40 and reserve the right to pursue the subject matter of claim 40 in a continuation or divisional application.

The claims have been amended to exclude ascorbic acid and to require "from 0.1% to 1.25% by weight of citric acid." Applicants have added claims 41 – 44 reciting the specific formulations of Examples 1-5, which lack ascorbic acid and each contain 0.25% citric acid.

Applicants have found no source of motivation in the cited references to lead a person of ordinary skill in the art to the subject matter of the presently claimed invention.

Simvastatin is known to be relatively unstable in pharmaceutical compositions and to respond unpredictably to stabilizing agents. Ascorbic acid is known to successfully stabilize simvastatin in pharmaceutical compositions. However ascorbic acid introduces undesirable discoloration in pharmaceutical compositions; this generally necessitates a film coating to mask the discoloration (specification, p. 5, ll. 23-25).

The cited references do not disclose or suggest that a relatively small amount of citric acid as claimed would provide sufficient stability, while avoiding discoloration associated with ascorbic acid. The discoloration is unacceptable in a commercial formulation. Consequently, formulations with ascorbic acid required a film coating to mask the discoloration. As explained in the specification (p. 5, lines 5-8 and 20-28) ascorbic acid is a stabilizing agent that causes discoloration. The applicants have found that the claimed formulation provides sufficient stability without ascorbic acid to eliminate the need to include an outer film coat to mask discoloration.

Applicants note that U.S. Patent No. 6,218,403 ("Daste et al.") (cited on sheet 2 of the form PTO/SB/08A currently of record) discloses simvastatin formulations in Examples 1-2 (cols. 9-10) with both citric acid and ascorbic acid. However Daste et al. does not suggest that a simvastatin-ezetimibe formulation with from 0.1% to 1.25% by weight of citric acid would provide sufficient stability, absent ascorbic acid and associated disadvantageous discoloration.

The applicants have surprisingly found that the present invention as claimed and as embodied in Examples 1-5 (pp. 12-14), provides stability against discoloration without ascorbic acid and with only relatively small amounts of citric acid. A skilled artisan in possession of Daste et al. would expect that upon omitting ascorbic acid, the simvastatin would not be predictably stabilized, or at least that the amount of citric acid must be correspondingly increased. The applicants have surprisingly found neither expectation to be the case. Accordingly, the invention as presently claimed would not have been obvious to a person of ordinary skill in the art at the time of the invention.

For the reasons provided above, Applicants submit that the present claims are allowable in all respects.

IV. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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